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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/618,178	07/18/2000	Stephen E. Lincoln	13151-2	9015

23719 7590 02/21/2008
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EXAMINER	
MUMMERT, STEPHANIE KANE	
ART UNIT	**PAPER NUMBER**
1637	

MAIL DATE	DELIVERY MODE
02/21/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/618,178	LINCOLN ET AL.	
	Examiner	Art Unit	
	Stephanie K. Mummert, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *75,76,78-82,85-87,91-98,100,102 and 106-115* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *75,76,78-82,85-87,91-98,100,102 and 106-115* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/30/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Examiner of record has changed. Please address all future correspondence to Examiner Mummert, whose contact information is included at the conclusion of this communication.

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on October 30, 2007 has been entered.

Status of Claims

Claims 1-74, 77, 83-84, 88-90, 99, 101, 103-105 have been canceled. Claims 75-76, 78-82, 85-87, 91-98, 100, 102, 106-115 are pending.

Claims 75-76, 78-82, 85-87, 91-98, 100, 102, 106-115 are discussed in this Office action.

All of the amendments and arguments have been thoroughly reviewed and considered but are not found persuasive for the reasons discussed below. Any rejection not reiterated in this action has been withdrawn as being obviated by the amendment of the claims. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This action is made FINAL (for reasons stated at the conclusion).

Information Disclosure Statement

The information disclosure statement (IDS) submitted on October 30, 2007 was filed in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Previous Grounds of Rejection

The rejection of claim 94 is withdrawn in view of Applicant's arguments.

Priority

Applicant's claim of priority back to application 08/173,173, 07/775,786 and 07/664,837 is noted. The examiner was unable to determine whether these applications provide support for the entirety of the current claims and therefore the claims are given the effective date of the immediate parent 09/088,820, which provides express support (except for claim 50, as detailed below).

Note - the statement of rejections for Kimpton, Ledwina and Jean-Pierre and those that depend from it have been corrected to remove cancelled claim 77.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 75-76, 78-82, 85, 86, 91-93, 95, 96-98, 102, 106-109 and112-115 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kimpton et al (PCR Meth. Appl. (August 1993) 3:13-22) in view of Ledwina et al (Biometrics (1980) 36:161-165) and further as motivated in view of JeanPierre (Ann. Hum. Genet. (1992) 56:325-330).

Kimpton teaches a method of claims 75 and 96 of determining the genotype at a locus within genetic material obtained by PCR amplification from a subject (page 14) comprising:

a) Reacting the material at the locus to produce a first reaction value (see page 14, columns 1-3, subheading "Locus specific amplification conditions"),

b) forming a data set including the first reaction value by assembling reaction value data points for the samples, each reaction-value data point corresponding to a respective one of the samples and including at least one reaction value (here the data points represented by each of the separate peaks in figure 1 represents a different sample and are assembled in figure 2) (see pages 14-16),

e) determining the genotype and confidence score for each reaction value data point, thus determining the genotype and confidence score at the genetic locus for each sample (here, table 2 on page 17 provides for each reaction point the genotype and a standard deviation based on the data obtained from step d) (page 16 and page 17).

With regard to claim 78, Kimpton expressly teaches reacting the material at multiple loci (page 14, table 1).

With regard to claims 80-82, 114, 115, on page 17, Kimpton expressly considers multiple alleles in the probability distributions, particularly in table 2 which expressly notes that the method is applicable to any number of alleles.

With regard to claim 85, 97, 98, 108, 109, Kimpton teaches confidence score determination (see pages 16 and 17).

With regard to claim 86, 102, 107, Kimpton expressly selected the loci for their discrimination ability and teaches that several different loci may be analyzed (page 16, column 1).

With regard to claims 91-93, Kimpton expressly teaches the use of multiple data points derived from multiple runs of the automated apparatus including multiple data sets in the exemplified method and apparatus (page 16, especially figure 2).

With regard to claim 95, Kimpton expressly teaches that the locus may be dinucleotide or tetranucleotide repeats (page 13).

With regard to claim 112, Kimpton teaches obtaining data that correlates the reaction value to the genotype (see pages 16 and 17).

With regard to claim 113, Kimpton demonstrates optical signals (see figure 1, where dye labeled DNA products are detected).

While Kimpton uses the Hardy-Weinberg test, Kimpton does not establish a distribution set of probability distributions and Kimpton does not then apply the reaction value of the distributions to detemine a measure of a conditional probability of each genotype of interest at the locus.

Ledwina teaches a method in which genotypes can be determined in which the Hardy Weinberg test is modified such that the steps of:

c) establishing a distribution set of probability distributions and associating hypothetical values with corresponding probabilities for each genotype of interest (see page 162 and page 163),

d) applying the first value to each pertinent probability distribution to determine a measure of conditional probability of each genotype of interest (see page 162 and page 163, especially "conditional distribution of T given Z=z" equation on page 163).

With regard to claim 76 and 79, Ledwina teaches a plurality of distributions which are hypothetical (see page 162, "common probability distribution of (T,Z) is multinomial with 1/2m(m+1) cells and with the vector of cell probabilities g=(g...).".

Further, JeanPierre motivates the use of computation of unknown genotypes to analyze the conditional probabilities relative to a distribution of hypothetical reaction values (see page 330).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Kimpton to use the conditional probability distribution method of Ledwina since Kimpton notes that the anlaysis uses the Hardy-Weinberg equilibria (see abstract) and since Ledwina states "The class of admissible tests for Hardy-Weinberg equilibrium in a multi allelic system is characterized. The standard goodness of fit chi square test is shown to be admissible for systems of two or more alleles. The conditional probability distribution required to determine the exact significance level of this test is presented (see abstract)". An ordinary practitioner would have been motivated to apply this hypothetical distribution analysis to genotyping since Jeanpierre notes the gains from creating such a distribution include avoiding hazards such as incorrectly using the simple average of the conditional probabilities instead of the harmonic mean, to more accurately determine the genotype (see page 330).

4. Claims 75-82, 85-87, 91-98, 100, 102, 106-115 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kimpton et al (PCR Meth. Appl. (August 1993) 3:13-22) in view of

Ledwina et al (Biometrics (1980) 36:161-165) and further as motivated in view of JeanPierre (Ann. Hum. Genet. (1992) 56:325-330) and further in view of Goulet et al.

Kimpton in view of Ledwina as motivated by JeanPierre teach the limitations of claims 75-76, 78-82, 85, 86, 91-93, 95, 96-98, 102, 106-109 and 112-115 as discussed above. Kimpton in view of Ledwina as motivated by JeanPierre does not teach genetic bit analysis, which includes allele specific amplification, nor the particular alleles listed.

Goelet teaches genetic bit analysis methods, including allele specific amplification methods (see entire document, expecially pages 10-13). Goulet teaches single specific nucleotide alleles (see page 40, example 3). Goulet also shows a mutation which is associated, at least indirectly, with a restriction site (see figure 2).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine the method of Kimpton in view of Clark with the use of genetic bit analysis or allele specific amplification to develop the data since Goelet states "The current invention provides a method that can be used to diagnose or characterize nucleic acids in biological samples without recourse to gel electrophoretic size separation of the nucleic acid species. This feature renders this process easily adaptable to automation and thus will permit the analysis of large numbers of samples at relatively low cost (page 8, lines 27-33)". An ordinary practitioner would have been motivated to substitute the equivalent genetic bit analysis method for PCR in order to minimize the need for gel electrophoresis and enhance the automatability of the process as expressly motivated by Goulet in order to speed analysis and minimize costs.

Response to Arguments

5. Applicant's arguments filed in the appeal brief filed November 17, 2006 and the reply brief filed April 12, 2007 have been fully considered but they are not persuasive.

6. The arguments made of record in the Examiner's Answer filed February 5, 2007 are incorporated herein by reference.

7. The arguments included within the reply brief have been considered. The arguments of record in the examiner's answer address these arguments as well, for the reasons stated above. However, particularly relevant passages of the arguments in the reply brief will be addressed briefly herein.

Applicant attempts to highlight purported errors in the examiner's answer and the arguments in support of the case for prima facie obviousness. These arguments by Applicant are directed largely to the arguments without considering the arguments in light of the teachings of the references as set forth in the grounds of rejection. Applicant argues that Kimpton does not teach limitation B, as noted in the chart included in the examiner's answer. It is noted in response that Kimpton clearly teaches a data set including reaction values as pointed out in the art rejection, specifically Figures 1 and 2 and page 14 of Kimpton.

/ This portion of Kimpton also addresses Applicant's repeated argument that Kimpton contains no indication that "the data sets referred to in the quoted passage included or could be deconstructed to retrieve a particular measured electrophoretic band size for a particular individual who had been assigned a given allelic designation number" (p. 4 of reply brief). Applicant is ignoring that Kimpton clearly starts with data that is provided from individual blood samples, that is amplified using the STR markers (Figure 1), which is then compiled into frequency distributions. While Kimpton does not indicate that the individual data could or would be deconstructed from the final result, it is clear that Kimpton works from the individual information up to the larger allelic distrubtion, so this deconstruction would not be necessary.

Throughout the reply brief, Applicant also argues that "Kimpton et al. publication does not disclose suggest or motivate, but affirmatively teaches away from the method of claim 75 of the subject application for determining the genotype of a subject at a locus" (p. 3 of remarks). This argument is not persuasive.

As cited by Applicant at page 9 of the reply brief, Kimpton distinctly teaches the applicability of the method to the identification of individuals:

> Prior to routine use of these loci by forensic laboratories for the identification of individuals, it must be confirmed that the detection and sizing protocols used allow accurate, reliable, and unambiguous allele designation.

This is an explicit statement by Kimpton to apply their method to determining the genotype of an individual subject at a locus. Therefore, Applicant's arguments regarding a lack of motivation are not persuasive.

Finally, regarding this same passage of Kimpton and the assertion by the Examiner that the passage motivates further statistical analysis by the addition of the Ledwina and Jean-Pierre references, Applicant argues that the portion of Kimpton referring to the reduced level of stuttering for tri and tetra nucleotide repeats "reiterates and confirms other disclosures in the publication that, in the analytical method of the publication, short-tandem-repeat loci with three or four base-pair repeat units could be selected to permit precise, unambiguous allele designation using polyacrylamide gels".

These arguments are not persuasive. As Applicant notes, the passage above beginning "prior to routine use of these loci..." refers specifically to HUMAPOA11 and HUMACTBP2. A careful review of the Kimpton publication and the associated references shows that HUMACTBP2 is a tetranucleotide repeat and HUMAPOA11 is a trinucleotide repeat (see

references 33, 34 for HUMACTBP2 and references 35, 36 for HUMAPOA11 in Table 1). Therefore, considering the statements by Kimpton regarding the need for further analysis of these markers does not mesh with Applicant's conclusion that the inclusion of tri and tetranucleotide repeats yields "precise, unambiguous allele designations" without fail is incorrect. The statements notes above regarding Kimpton provide explicit teaching, suggestion and motivation for the application of further statistical analysis to the method as taught by Kimpton, particularly when the method is applied in a forensic setting for the genotyping of individuals.

Conclusion

This is a continuation of applicant's earlier Application No. 09/618178. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however,

event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

No claims are allowed. All pending claims stand rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephanie K. Mummert, Ph.D. whose telephone number is 571-272-8503. The examiner can normally be reached on M-F, 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Stephanie K. Mummert

Stephanie K Mummert, Ph.D.
Examiner
Art Unit 1637

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